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1879 '00 APR 14 A10:33

March 30, 2000

**Robert S. Stern, M.D.**
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RE: Docket 39D5435 Draft Guidance for Industry on Photo Safety Testing.

Dockets Management Branch
(HFA 305)
Food & Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD
20852

To Whom It May Concern:

I believe that the Draft Guidance criteria to guide which compounds would require specific photo safety testing, particularly testing for the effects of photo-carcinogenesis, omitted at least three potentially important criteria in determining whether or not a compound would need a fuller assessment in laboratory, animals, or through human investigational or epidemiological studies. These three additional criteria are site of application of the product, age of patients most likely to use of the product, and whether the product is likely to be disproportionately used by patients with past exposures or attributes more likely to put them at higher risk for skin cancer. Below I provide examples of situations and/or products that might merit particular scrutiny for photo-safety and particularly photo-carcinogenicity testing, that, in my reading, were not as explicitly addressed in the draft guidance of January, 2000, as might be desirable.

The first criteria that might be suggest special attention to evaluation of photo-carcinogenic effects would be sites of application. Clearly, a product that is likely to be used to substantial extent on exposed areas, particularly the head and neck, which are the primary sites for photo-carcinogenicity for non-melanoma skin cancer, might merit greater scrutiny than one that is much more likely to be applied to other body sites. An example of such a product might be a topical anti-inflammatory/immunosuppressive drug which was not a corticosteroid and might be preferentially used on the face because of its lack of atrophogenic effects.

The second criteria would be age of use. Multiple epidemiologic studies indicate that exposure to younger persons to UV is a more important risk factor for non-melanoma skin cancer than exposure in later life. Therefore, products that are likely to be used in younger persons, particularly those under 20 and particularly on sun exposed areas should merit especially careful evaluation for photo-carcinogenic properties. Again, for example, a product for eczema that has an advantage over a topical corticosteroids with respect to atrophic effects, but might have immunosuppressive effects that can ultimately lead to enhanced carcinogenic risk, would appear to merit particularly close scrutiny.

A third consideration would be products intended for populations in particularly high risk. Here, the classic example would be immunosuppressive drugs for the treatment of severe psoriasis. Given that patients with severe psoriasis are very likely to have been

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exposed to multiple carcinogens, such as PUVA and Ultraviolet B and tar, perhaps even transient drug induced immunosuppressive therapy, might lead to both substantially higher relative and absolute increases in risk of skin cancer than that observed with the use of these agents in other populations, such as transplant recipients or persons with arthritis that lack such extensive prior exposure to carcinogenic agents.

Thank you for the opportunity to comment on this draft guidance.

Sincerely yours,

Robert S. Stern, M.D.

RSS/tjc

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